A Phase II Randomized Trial of Recombinant Fowlpox that Expresses PSA in Patients with Adenocarcinoma of the Prostate.

Vaccinia virus has been used as an immunotherapy vaccine to produce cellular and humoral responses to tumor associated antigens in human cancer. Recombinant vaccinia (rV) virus vectors engineered to contain genomic sequences to carcinoembryonic antigen (CEA), prostate specific antigen (PSA), and MUC1/ interleukin-2 (IL-2) have been safely administered to patients with advanced cancer with the development of specific cytotoxic T lymphocytes (CTLs) against the target antigen with evidence of clinical disease stabilization. PSA is expressed in most human prostate cancers. A recombinant vaccinia virus, which expresses the human PSA gene, has been administered to 33 patients at the Harvard/Boston Phase I Oncology Group member institutions. No vaccinia related toxicity has been encountered in any patient. Thirteen of 33 patients remain on study (without a greater than 50% rise in serum PSA for three consecutive months) for 2-22+ months. Fowl pox is a pox virus which does not replicate in humans. Like vaccinia, the fowl pox genome can be manipulated to contain human DNA sequences (rF). In mice, a combination of rV and rF vaccines to a tumor specific protein was superior to either vaccine alone.

In this randomized Phase II trial, an initial cohorts of patients will receive three monthly injections of 1.5×10^8 and 1.5×10^9 plaque forming units (pfu) of rF-PSA. Escalations will proceed in the absence of dose limiting toxicity. Patients will monitored for clinical response and serologic response (PSA). Immunologic response will be measured by the titer of CTLs produced with serial vaccinations. When a safe dose has been established, additional patients will be randomly allocated to one of 2 sequences of rF-PSA followed by rV-PSA (2.65×10^8 pfu) or the reverse. Immunologic responses and serum PSA will be followed as will time to disease progression-either a greater than 50% rise in serum PSA for three consecutive months or the development of clinical disease progression.